In re Application of: Yoseph Shaaltiel
Serial No.: 10/554,387
Filed: October 25, 2005
Office Action Mailing Date: January 9, 2008

Examiner:FRONDA
Group Art Unit: 1652
Attorney Docket: 30570

In the Claims:

Please cancel claims 1-72 and replace them with new claims 73-141, as follows.

1-72.Canceled

73.(New) An isolated nucleic acid sequence encoding a human lysosomal protein being contiguously linked to a C-terminal vacuolar targeting signal and an N-terminal endoplasmic reticulum signal peptide.

74.(New) An isolated nucleic acid sequence encoding a human lysosomal protein being contiguously linked to a C-terminal endoplasmic reticulum retention signal and an N-terminal endoplasmic reticulum signal peptide.

75.(New) The isolated nucleic acid sequence of claim 73, wherein wherein said human lysosomal protein is a glucocerebrosidase.

76.(New) The isolated nucleic acid sequence of claim 73, wherein said human lysosomal protein is a human α-galactosidase.

77.(New) The isolated nucleic acid sequence of claim 74, wherein said human lysosomal protein is a human glucocerebrosidase.

78.(New) The isolated nucleic acid sequence of claim 74, wherein said human lysosomal protein is a human α-galactosidase.

79.(New) The isolated nucleic acid of claim 73, wherein said vacuolar targeting signal is a basic tobacco chitinase A gene vacuolar targeting signal.

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80.(New) The isolated nucleic acid of claim 79, wherein said vacuolar targeting signal is as set forth in SEQ ID NO: 2.

81.(New) The isolated nucleic acid of claim 73, wherein said endoplasmic reticulum signal peptide is as set forth in SEQ ID NO: 1.

82.(New) The isolated nucleic acid of claim 73, wherein said human lysosomal protein comprises an amino acid sequence as set forth in SEQ ID NO: 8.

83.(New) The isolated nucleic acid of claim 73, wherein said nucleic acid sequence is as set forth in SEQ ID NO: 7.

84.(New) The isolated nucleic acid of claim 73, wherein said nucleic acid sequence is as set forth in SEQ ID NO: 13.

85.(New) The isolated nucleic acid of claim 73, further comprising a promoter functional in plant cells transcriptionally linked to said nucleic acid sequence.

86.(New) The isolated nucleic acid of claim 85, wherein said promoter sequence is a Cauliflower Mosaic Virus S-35 promoter sequence.

87.(New) The isolated nucleic acid of claim 73, further comprising a transcriptionally linked terminator sequence functional in plant cells.

88.(New) The isolated nucleic acid of claim 73, wherein said isolated nucleic acid sequence optionally further comprises additional operably linked control, promoting and regulatory elements and/or selectable markers.

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89.(New) The isolated nucleic acid of claim 88, wherein said terminator is an octopine synthase terminator of *Agrobacterium tumefaciens*, and the regulatory element is the TMV (Tobacco Mosaic Virus) omega translational enhancer element.

90.(New) A nucleic acid construct capable of expression in a plant cell comprising the isolated nucleic acid of claim 73.

91.(New) A cell comprising the nucleic acid construct of claim 90.

92.(New) The cell of claim 91, recombinantly producing said human lysosomal enzyme.

93.(New) The cell of claim 92, wherein said human lysosomal protein is recombinantly produced so as to have at least one xylose and at least one exposed mannose residue.

94.(New) The cell of claim 91, wherein said cell is a plant cell.

95.(New) The cell of claim 94, wherein said plant cell is a plant root cell selected from the group consisting of *Agrobacterium rihzogenes* transformed root cell, celery cell, ginger cell, horseradish cell and carrot cell.

96.(New) The cell of claim 95, wherein said plant cell is a carrot cell.

97.(New) The cell of claim 91, wherein said cell is an *Agrobacterium tumefaciens* cell.

98.(New) A human lysosomal protein comprising at least one xylose residue and at least one exposed mannose residue.

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99.(New) A human lysosomal protein comprising at least one exposed mannose residue and at least one fucose residue having an alpha (1-3) glycosidic bond.

100.(New) The human lysosomal protein of claim 98, further comprising at least one fucose residue having an alpha (1-3) glycosidic bond.

101.(New) The human lysosomal protein of claim 99, further comprising at least one xylose residue.

102.(New) The human lysosomal protein of claim 98, wherein said lysosomal enzyme is a glucocerebrosidase.

103.(New) The human lysosomal protein of claim 98, wherein said lysosomal enzyme is an α-galactosidase.

104.(New) The human lysosomal protein of claim 98, wherein said human lysosomal protein is contiguously linked to a C-terminal vacuolar targeting signal.

105.(New) The human lysosomal protein of claim 98, wherein said human lysosomal protein is contiguously linked to a C-terminal vacuolar targeting signal and an N-terminal endoplasmic reticulum signal peptide.

106.(New) The human lysosomal protein of claim 105, wherein said vacuolar targeting signal is a basic tobacco chitinase A gene vacuolar targeting signal.

107.(New) The human lysosomal protein of claim 106, wherein said vacuolar targeting signal is as set forth in SEQ ID NO: 2.

108.(New) The human lysosomal protein of claim 105, wherein said endoplasmic reticulum signal peptide is as set forth in SEQ ID NO: 1.

109.(New) The human lysosomal protein of claim 102, wherein said human glucocerebrosidase comprises an amino acid sequence as set forth in SEQ ID NO: 8.

110.(New) The human lysosomal protein of claim 98, wherein said lysosomal protein having a biological activity.

111.(New) The human lysosomal protein of claim 98, wherein said biological activity is uptake into macrophages.

112.(New) The human lysosomal protein of claim 98, wherein said biological activity is enzymatic activity.

113.(New) The lysosomal protein of claim 111, having an increased affinity for said macrophages, in comparison with the corresponding affinity of a naturally occurring lysosomal protein to said macrophages.

114.(New) A pharmaceutical composition comprising the human lysosomal protein of claim 99 and a pharmaceutically acceptable carrier.

115.(New) A plant cell preparation comprising a human lysosomal protein comprising at least one xylose residue and at least one exposed mannose residue.

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116.(New) A plant cell preparation comprising a human lysosomal protein comprising at least one exposed mannose residue and at least one fucose residue having an alpha (1-3) glycosidic bond.

117.(New) The plant cell preparation of claim 115, further comprising at least one fucose residue having an alpha (1-3) glycosidic bond.

118.(New) The plant cell preparation of claim 116, further comprising at least one xylose residue.

119.(New) The plant cell preparation of claims 115, wherein said lysosomal protein is a human glucocerebrosidase.

120.(New) The plant cell preparation of claim 115, wherein said human lysosomal protein comprises an amino acid sequence as set forth in SEQ ID NO: 8.

121.(New) The plant cell preparation of claim 115, wherein said lysosomal protein is a human α-galactosidase.

122.(New) The plant cell preparation of claim 115, wherein said human lysosomal protein is contiguously linked to a C-terminal vacuolar targeting signal

123.(New) The plant cell preparation of claim 115, wherein said human lysosomal protein is contiguously linked to a C-terminal vacuolar targeting signal and an N-terminal endoplasmic reticulum signal peptide.

124.(New) The plant cell preparation of claim 122, wherein said vacuolar targeting signal is a basic tobacco chitinase A gene vacuolar targeting signal.

125.(New) The plant cell preparation of claim 122, wherein said vacuolar targeting signal is as set forth in SEQ ID NO: 2.

126.(New) The plant cell preparation of claim 123, wherein said endoplasmic reticulum signal peptide is as set forth in SEQ ID NO: 1.

127.(New) The plant cell preparation of claim 115, wherein said human lysosomal protein having at least one exposed mannose residue comprises a dominant fraction of said lysosomal protein, as measured by linkage analysis.

128.(New) A pharmaceutical composition comprising the plant cell preparation of claim 115 and a pharmaceutically acceptable carrier.

129.(New) A method of producing a lysosomal protein comprising:

preparing a culture of recombinant cells transformed or transfected with the nucleic acid construct of claim 90; and

culturing said cell culture under conditions permitting the expression of said protein, wherein said protein produced by said cells comprises at least one xylose residue.

130.(New) The method of claim 129, wherein said cell culture is cultured in suspension.

131.(New) The method of claim 129, further comprising:

purifying said protein.

132.(New) The method according to claim 129, wherein said protein produced by said cell has at least one xylose and at least one exposed mannose residue.

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133.(New) The method according to claim 131, wherein said lysosomal protein binds to a mannose receptor on a macrophage.

134.(New) The method according to claim 129, wherein said lysosomal protein has increased affinity for said macrophage, in comparison with the corresponding affinity of a naturally occurring lysosomal protein to said macrophage.

135.(New) Use of a biologically active lysosomal enzyme as defined by claim 110, in the manufacture of a medicament for the treatment or prevention of a lysosomal storage disease.

136.(New) The use of claim 135, wherein said lysosomal enzyme has increased affinity for macrophage cells, in comparison with the corresponding affinity of a naturally occurring lysosomal enzyme to said macrophage cells.

137.(New) The use according to claim 135, wherein said disease is Gaucher's disease.

138.(New) A method for treating a subject having lysosomal storage disease using a biologically active recombinant lysosomal enzyme, comprising:

(a) providing a recombinant biologically active lysosomal enzyme as defined in claim 110; and

(b) administering a therapeutically effective amount of said recombinant biologically active lysosomal enzyme to said subject.

139. (New) The method according to claim 138, wherein said lysosomal enzyme is glucocerebrosidase (GCD).

140. (New) The method according to claim 138, wherein said lysosomal storage disease is Gaucher's disease.

141. (New) The method according to claim 138, wherein said target cell at the target site is a Kupffer cell in the liver of said subject.